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Does the Current Consent Process Minimize the Risks of Genetics Research?

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Completion of the human genome project is expected to lead to an increase in the number of individuals who participate in genetics research. The current informed consent process—developed prior to widespread genetics research—may not be sufficient to minimize the research risks that these individuals face. The current consent process focuses on informing individuals of the risks of research participation prior to their research enrollment. However, the risks of genetics research often are influenced by what subjects disclose to others after their research participation has ended. To assess whether the current consent process helps subjects remember the risks of future disclosures and, thereby, minimize the risks of genetics research, we interviewed 130 individuals who had previously participated in genetics research. Nineteen percent recalled that their samples would undergo genetic testing; 16% recalled that samples might be used for future research; 15% recalled that release of research records could affect their insurance status. These data suggest that current consent practices may not minimize the risks of genetics research. To address this concern, Institutional Review Boards and investigators should consider implementing supplemental mechanisms to help subjects remember when forgetting aspects of their research participation could place them at increased risk.

KEY WORDS: future disclosure; recall

INTRODUCTION

Research on the genetic components of common diseases has increased dramatically, and more individuals now participate in genetics research. To ensure that these individuals are protected from research risks, it is important to consider whether current human subjects protections—developed prior to widespread genetic testing—are sufficient for genetics research. In particular, we consider whether the current consent process minimizes the risks of genetics research.

The current consent process was designed to provide potential subjects with the information they need to make a decision whether to enroll in research [Levine, 1986; Applebaum et al., 1987]. To this end, the Federal regulations (Common Rule, 45CFR46) require that clinical investigators inform potential subjects of eight central aspects of proposed research studies, including the risks [OPRR, 1991]. The Federal regulations do not require that investigators help subjects *remember* the risks of research participation. In most cases, this makes sense. The risks of research typically end when subjects' participation ends, thereby eliminating any need for subjects to remember the risks of their research participation. Even when subjects face a risk of future harm, say, the risk of future peripheral neuropathy, there is typically little they can do to reduce these risks.

The principal risks of genetics research, to employment, insurance, and personal relationships, are different in this regard because they arise *after* subjects' research participation has ended. It is the possibility that information about subjects' participation in genetics research may be disclosed to others that poses risks. Investigators can help to minimize these risks by protecting subjects' confidentiality. However, in some cases, the risks of genetic-research also depend on whether subjects themselves inform others, insurers, employers, physicians, or even relatives, about their research participation. For example, simply disclosing the fact that one participated in a genetics study related to Huntington's disease or Alzheimer disease could place one at increased risk [McEwan, 1998]. Also, depending upon the specific tests being conducted, disclosing testing results could introduce additional risks. The

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possibility that future disclosures can prove harmful raises a crucial question for genetics research: does the current consent process help subjects remember their research participation in a way that minimizes the potential for harmful, future disclosures?

METHODS

Assessment of Subject Recall

The research consent process includes both a written consent form and discussions with the research team. While discussions with the research team are not formalized, all subjects are required to receive and sign an Institutional Review Board (IRB)-approved, written consent form. Hence, we used the information included in the written consent form as the standard against which to assess subjects' recall. Specifically, we evaluated the content of the consent forms for two longitudinal studies related to Alzheimer disease, and assessed whether subjects recalled five central aspects of the genetic testing they underwent:

1. Genetic tests related to Alzheimer disease are available.
2. Samples were taken for genetics research on Alzheimer disease.
3. Testing for APOE alleles was performed.
4. Samples might be used for future research.
5. Release of research records could affect subjects' ability to obtain insurance.

We considered genetics research on Alzheimer disease a useful model to assess whether the current consent process helps subjects remember their research participation because the disease is so prevalent, affecting up to 10% of people aged 65 or older, and much research is devoted to identifying its genetic components [Evans, 1989; National Institute on Aging, 1997; Roses, 1998]. Moreover, caring for individuals with Alzheimer disease can be very costly, raising concerns about potential discrimination against those thought to be at increased risk for developing the disease.

Survey Respondents

Potential respondents were identified from longitudinal studies at Duke University and the National Institutes of Health (NIH) for people who have a first-degree relative with probable Alzheimer disease. To participate in these studies, individuals had to be free from Alzheimer disease as judged by the investigators. Both studies involved testing for apolipoprotein (APOE) alleles; neither provided subjects with their APOE test results.

Interviewers from the Center for Survey Research conducted the surveys over the telephone using a functional assessment of subjects' cognitive ability: those able to negotiate an interview time and remember the survey questions were deemed competent. Of the 134 individuals invited to participate, 130 completed the survey (response rate = 97.0%).

Statistical Analysis and Approvals

Associations of responses with demographic characteristics were tested using a multivariate logistic regression model and a Wald chi-square statistic. An overall test was first performed [alpha = 0.05] before individual factors were examined. This study was approved by the IRBs at Duke University and the National Institute of Mental Health.

Content Analysis of the Consent Forms

To assess whether the manner of presentation affects subjects' recall, we evaluated four characteristics of the two consent forms:

1. Length.
2. Number of pages devoted to the genetic testing.
3. Number of lines devoted to each of the five key aspects of the genetic testing.
4. The central statement regarding the five key aspects of the genetic testing, except for APOE testing where we evaluated how many times "APOE" was mentioned.

RESULTS

Respondents' Characteristics

Table I reports respondents' sociodemographics, and how long prior to the present survey they had enrolled in their respective longitudinal study. Overall, respondents were older, wealthier, and more educated than the general U.S. population [U.S. Census, 1999]. All respondents reported having enrolled in their respective longitudinal study within the previous 4 years, 40% within the previous 12 months.

TABLE I. Participants' Sociodemographics

	N = 130
Site	
Duke	48 (37%)
NIH	82 (63%)
Sex	
Male	51 (39%)
Female	79 (61%)
Age	
50–55	22 (17%)
55–64	64 (49%)
65–74	33 (25%)
≥75	11 (9%)
Income	
Don't know	3 (2%)
No answer	17 (13%)
<$25,000	11 (9%)
$25–$75,000	47 (36%)
>75,000	52 (40%)
Time since consented to longitudinal study	
<6 months	19 (15%)
6 months–1 year	35 (27%)
1–2 years	57 (44%)
2–4 years	19 (15%)

NIH, National Institutes of Health.

TABLE II. Content of Consent Forms

	Duke	NIH
Overall form	3 pages	8 pages
Genetic testing section	3 pages	3/4 page
Availability of genetic tests	5 lines	3 lines
	"Certain genes have been linked to Alzheimer disease."	"Genetic factors are certainly involved [in Alzheimer disease]."
Obtaining samples	8 lines	5 lines
	"I will be asked to give a sample of blood and a sample of cells from my inner cheeks."	"We would like to study genetic material [DNA] from you."
APOE testing	9 lines	3 lines
	Mentions "APOE" 14 times.	Mentions "APOE" 3 times.
Future research	8 lines	5 lines
	"My DNA may be retained indefinitely by this research group and analyzed as part of other research activities."	"For your information, we will also be saving samples for possible future testing."
Release of records	3 lines	5 lines
	"If genetic information were to be released to an insurance company or employer, it could have an impact on the ability to acquire or maintain life, health, and disability insurance."	"If you sign a release of information form for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect [either favorably or unfavorably] the willingness of the insurance company to sell you insurance."

APOE, apolipoprotein; NIH, National Institutes of Health.

Consent Forms for the Longitudinal Studies

At both sites, the IRB-mandated consent form was explained to subjects, who then signed and received a copy. Table II describes how the two consent forms explain the five identified aspects of the genetic testing. At the NIH, the genetics information was included in the consent form for the overall longitudinal study. This form was eight pages long and included three fourths of a page on genetic testing. At Duke, the genetics information was provided in a *separate* three-page form. Both forms explain each of the five identified aspects of the genetic testing: genetic tests related to Alzheimer disease are available, samples will be obtained, APOE testing will be conducted, samples may be used for future research, and release of records could affect subjects' ability to obtain insurance.

Respondents' Recall

Table III reports the percentage of respondents who recalled each of the five identified aspects of the genetic testing. Respondents who did not remember that their DNA had been tested at all were not asked whether they recalled the specific aspects of this testing. Hence, our data assume that individuals who did not recall that their DNA was tested would not recall that:

1. Their DNA was tested specifically for APOE.
2. The sample of DNA that was tested might be used for future research.
3. Disclosure of the results of the testing could affect their ability to obtain insurance.

All respondents recalled participating in their respective longitudinal study. Fifty-eight percent recalled that genetic tests related to Alzheimer disease are available. Thirty-seven percent remembered that they had provided a sample for genetic testing. Nineteen percent recalled that the sample they had provided would be tested for APOE alleles. Sixteen percent recalled that this sample might be used for future research. Fifteen percent recalled that disclosure of research records could affect their ability to obtain insurance. There were no statistically significant differences in recall on any of the five measures between the NIH and

TABLE III. Participants' Recall

N = 130	Yes	No	NA
Recall availability of genetic tests?	75 (58%)	54 (42%)	1 (1%)
Recall samples obtained?	48 (37%)	62 (48%)	20 (15%)
Recall APOE testing?	25 (19%)	101 (78%)	4 (3%)
Recall sample might be used for future research?	21 (16%)	109 (84%)	0
Recall that release of records could affect insurance?	20 (15%)	106 (82%)	4 (3%)

APOE, apolipoprotein.

Duke respondents. Furthermore, there were no statistically significant differences in recall on the five measures between respondents who had enrolled in their respective longitudinal study within the previous 6 months versus those who had enrolled in the previous 2–4 years.

DISCUSSION

We assessed the extent to which the current, Federally mandated consent process helps subjects remember five key aspects of their participation in genetics research. The results suggest that the current consent process does not help subjects remember these items. Slightly more than half of the respondents recalled that genetic tests related to Alzheimer disease are available; approximately one third recalled that they provided a sample for such research. Less than one in five remembered the kind of testing their sample underwent, that their sample could be used for future research, and that release of research records could affect their ability to obtain insurance. These findings raise a question of whether IRBs and genetics researchers should take steps to help subjects remember key aspects of their participation in genetics research.

Some might argue that forgetting one's participation in genetics research may protect subjects by eliminating the possibility that they will disclose the forgotten information. However, although respondents forgot key aspects of their participation, including the risks of future disclosures, they remembered having participated in genetics research related to Alzheimer disease. This pattern of remembering suggests that the current consent process, with its focus on informing subjects prior to research enrollment, may not help subjects remember the risks of future disclosures.

Presumably, IRBs and investigators should consider implementing supplemental mechanisms to help subjects remember the risks of future disclosures only when forgetting could place them at increased risk. In this regard, we assume there should be consistency between what subjects are told prior to enrollment, and what they are encouraged to remember after participation ends. When future disclosures would not place subjects at increased risk, there is no need to inform them of these theoretical risks before they enroll, and no need to remind them after their participation ends. However, when IRBs judge that future disclosures could place subjects at increased risk, informing them of these risks before they enroll in a particular study may not be sufficient to minimize the risks of genetics research; IRBs should also consider steps to help subjects *remember* these risks.

At present, the magnitude and likelihood of the risks of future disclosures are unknown. In particular, we did not assess the extent to which future disclosures might place those who participated in the longitudinal studies at increased risk. In the absence of general risk estimates, IRBs and genetics researchers should assess, on a protocol-by-protocol basis, the extent to which forgetting key aspects of one's participation in genetics research may place subjects at increased risk: Would forgetting aspects of *this* study introduce increased risks? When addressing this question, IRBs and investigators should recognize that subjects may be especially likely to forget past genetics research since participation often involves little more than an uneventful blood draw.

Currently, there are no data on what mechanisms might improve subjects' recall. The fact that respondents from Duke did not show better recall than the NIH respondents, despite use of a separate genetics consent form, suggests that this approach may not be sufficient. Similarly, respondents' failure to recall despite receiving a copy of the consent form suggests this practice may be insufficient as well. One possibility would be to develop a separate information sheet that includes only the items that subjects need to remember, and emphasizes the importance of remembering them. This sheet could be provided and explained to subjects at the end of their research participation or, for extended studies, several weeks after enrollment.

Respondents were not provided with their APOE test results, a common practice intended to protect subjects from misinterpreting research results of uncertain clinical significance. At the same time, providing results may help subjects remember, particularly if results are provided by a genetic counselor who explains the risks and provides strategies for avoiding harmful disclosures. If subjects continue to forget the risks of disclosure, despite such efforts, the provision of results could *increase* the risks of genetics research by increasing the information that subjects may disclose.

Another possibility would be to provide information about subjects' research participation to their physicians, who could then help subjects avoid harmful disclosures. Pursuit of this strategy should recognize the possibility that the placement of research information in patients' clinical charts may increase risks. Empirical research will be needed to assess whether these methods or other steps such as computer-assisted consents [Green and Fost, 1997] might help minimize the risks of future disclosures.

Four potential limitations should be noted. The present findings are limited to individuals who participated in research on Alzheimer disease. It can be argued that such individuals may be less at risk of discrimination because Alzheimer disease is so prevalent and tends to affect older individuals who are at lower risk of employment and insurance discrimination. However, two thirds of our respondents were of working age (under 65), and only 15% remembered that the release of research records could pose risks. Future research will be needed to determine the extent to which the current findings generalize to other groups.

Since respondents were significantly wealthier and better educated than the average American, our results may not be generalizable. However, wealthier and better-educated individuals do not seem less likely to remember. Next, respondents' family history of Alzheimer disease may raise concerns about whether their failure to remember is due to early dementia. Against this, respondents were judged to be free of the disease by Alzheimer disease experts at the time of enrollment, and periodically during their longitudinal study. Moreover,

they were assessed to be functionally competent at the time of the present survey.

Finally, we did not assess whether respondents *understood* the five identified key aspects at the time they consented to their longitudinal study. Thus, respondents' failure to recall may be due in part to their failure to understand initially. However, the assessed items, such as the statement that investigators would obtain a sample of subjects' blood, seem straightforward. Moreover, respondents were judged to understand these items at the time of the present survey.

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